EVALUATION BY MEANS OF GAS ANALYSIS, ON THE MEANING OF INTRAVENOUS LIPID INTAKE

by

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I. INTRODUCTION

Previously in our laboratory we succeeded in producing a fat emulsion (Fatgen) which could be safely given intravenously. SHIGENAGA in our laboratory investigated tissue metabolism following the intravenous administration of this fat emulsion into rats, by using WARBURG's apparatus. When carbohydrate, protein and fat are oxidized in the body, O_2-uptake and CO_2-evolution differ according to the foodstuffs. They are both measured easily by analyzing the respiratory air. HELMUT MÜLLER advocated calling the amount of O_2 needed to oxidize completely the metabolic intermediates excreted in the urine, Vakat-0. The author has attempted to investigate fat metabolism in vivo by means of gas analysis during intravenous administration of the fat emulsion, and by measuring the Vakat-0 and Vakat-0/N (N···quantity of nitrogen in urine).

II. MATERIALS AND METHODS

1) Fat Emulsion : In the present investigation, 20 % sesame oil emulsion which had been produced in our laboratory was used. This fat emulsion was infused intravenously into rabbits in the amount of 0.5g of fat per kg.

2) Experimental Animals : Adult male rabbits, each weighing approximately 2.5 kg were used. They had been maintained on a fixed diet for more than 3 weeks so that they attained a steady weight at the time of the experiment. In order to

Table 1 Changes in the value of R. Q. during urethane narcosis on rabbits

Time after infusion		0	1hr.	3 hrs.	6 hrs.	9 hrs.	12 hrs.
No. 1	O_2	15.0938	15.1452	14.9450	15.5073	15.0803	15.3792
	CO_2	14.2365	14.3038	14.0622	14.6308	14.2279	14.5461
	R. Q.	0.9432	0.9444	0.9409	0.9431	0.9434	0.9458
No. 3	O_2	14.2846	14.3622	14.0940	14.2245	14.2245	13.9980
	CO_2	13.2990	13.3717	13.1220	13.2435	13.2435	12.9935
	R. Q.	0.9310	0.9310	0.9310	0.9310	0.9310	0.9285
No. 4	O_2	14.7631	14.8230	14.6740	14.9170	14.8027	14.4380
	CO_2	13.6692	13.7259	13.5870	13.8120	13.7062	13.3740
	R. Q.	0.9259	0.9259	0.9259	0.9259	0.9259	0.9230

collect the respiratory air of rabbits they must be kept quiet under the same physiological conditions for a long time. For that reason, 20 % urethan solution was injected subcutaneously into rabbits in a dose of 0.5 g of urethan per kg. And 30 minutes later, they were fixed on a table and samples of respiratory air were collected successively. As shown in Table 1, no inconvenience due to the injection of urethan solution occurs in this experiment.

3) Drugs Used: Methionine as *l*-methionine, vitamin C as *l*-ascorbic acid, vitamin B_2 as riboflavin-5′-phosphate, pantothenic acid as calcium pantothenate and vitamin B_1 as thiamin hydrochloride were used.

4) Determination of the Quantity of Nitrogen in Urine and of Vakat-O: Urinalysis was performed every morning. Nitrogen in urine excreted during 24 hours was determined by KJELDAHL's method, and Vakat-O was determined by KANITZ's method.

III. RESULTS AND DISCUSSION

1) CHANGES IN O_2-UPTAKE, CO_2-EVOLUTION AND RESPIRATORY QUOTIENT (R. Q.) FOLLOWING THE INTRAVENOUS ADMINISTRATION OF FAT EMULSION

(i) Infusion of 7 % Glucose Solution Alone

With the intravenous infusion of sesame oil emulsion containing 7 % glucose, an increase in total oxygen consumption caused by oxidation of glucose itself would be expected. Therefore, first the changes in O_2-uptake and R. Q. etc. following a single infusion of glucose solution alone must be measured. So, the same amount of glucose as is contained in the 20 % sesame oil emulsion was dissolved in distilled water and injected intravenously into rabbits. The changes in O_2-uptake, CO_2-evolution and R. Q. were measured. As shown in Table 2 and Fig. 1, O_2-uptake began to increase immediately and reached its maximum 1 hour after the infusion and then decreased gradually. The value of R. Q. in this case was not so different from that before infusion. Therefore, in the use of glucose in such a small amount, it seems

Table 2 Changes in the value of R. Q. following single infusion of glucose solution into rabbits

Time after infusion		0	1 hr.	3 hrs.	6 hrs.
No. 5	O_2	14.4500	20.4645	17.3040	14.5283
	CO_2	13.6000	19.4900	16.5830	13.8966
	R. Q.	0.9411	0.9524	0.9583	0.9565
No. 7	O_2	13.0537	16.6060	13.9720	12.7596
	CO_2	12.0555	15.5272	13.1070	11.9697
	R. Q.	0.9311	0.9350	0.9380	0.9380
No. 8	O_2	15.8180	20.0713	17.0660	15.4160
	CO_2	15.0990	19.1986	16.8434	15.2233
	R. Q.	0.9545	0.9565	0.9820	0.9875
Mean	O_2 Change (%)	0	+ 31.90	+ 15.55	− 1.40
	R. Q.	0.9422	0.9422	0.9561	0.9606

that all of it is completely oxidized within a short time.

(ii) Infusion of 20 % Sesame Oil Emulsion Containing No Glucose

A 20 % sesame oil emulsion containing no glucose was especially prepared.

Fig. 1 Changes in the value of R. Q. and oxygen consumption following single infusion of glucose solution into rabbits

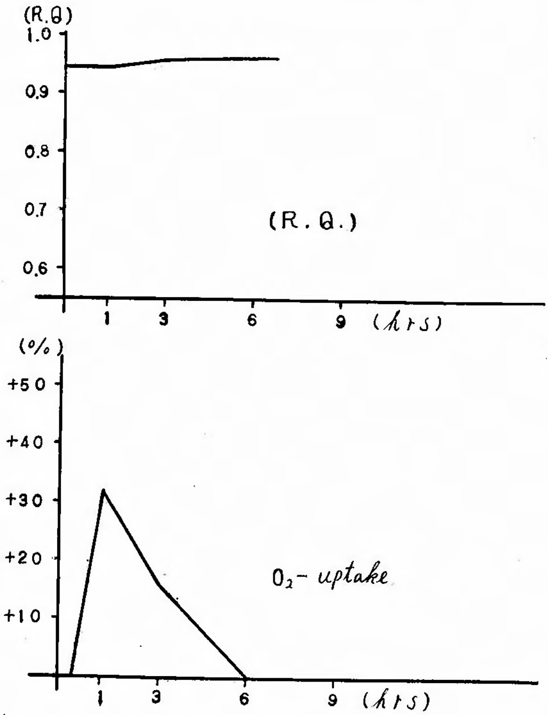


Fig. 2 Changes in the value of R. Q. and oxygen consumption following single infusion of 20% sesame oil emulsion containing no glucose into rabbits

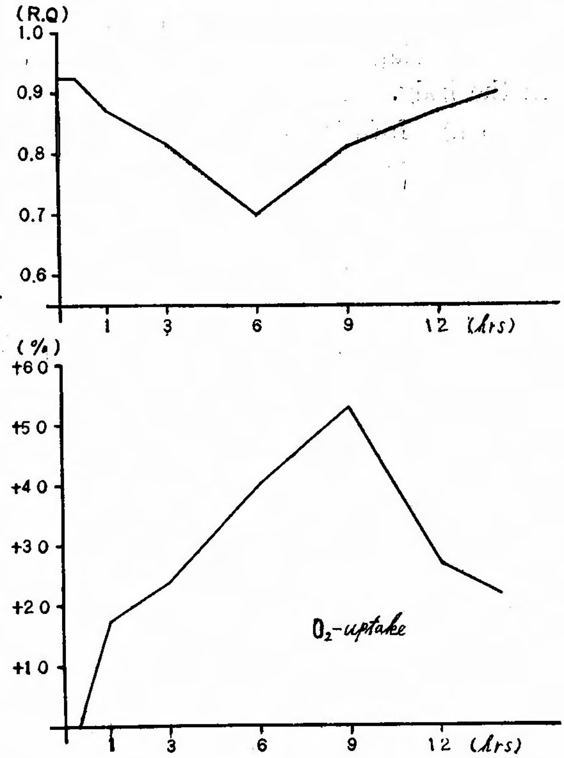


Table 3 Changes in the value of R. Q. following single infusion of 20% sesame oil emulsion containing no glucose into rabbits

Time after infusion		0	1 hr.	3 hrs.	6 hrs.	9 hrs.	12 hrs.
No. 9	O_2	14.8230	17.3940	18.1325	20.1795	23.2402	18.1090
	CO_2	13.7250	15.2190	15.0062	14.4925	19.5390	16.1687
	R. Q.	0.9259	0.8750	0.8275	0.7181	0.8407	0.8928
No. 11	O_2	14.3622	16.5925	17.6235	20.0960	22.2870	18.7546
	CO_2	13.3717	14.8541	14.7810	13.8160	17.6985	15.8690
	R, Q.	0.9310	0.8935	0.8387	0.6874	0.7941	0.8461
No. 12	O_2	17.3030	20.6335	21.8925	24.2325	25.9002	22.3355
	CO_2	15.9820	17.7875	17.5140	16.9627	20.8875	19.4535
	R. Q.	0.9230	0.8620	0.8000	0.7000	0.8064	0.8709
Mean	O_2 Change(%)	0	+ 17.39	+ 24.04	+40.64	+ 53.87	+ 27.27
	R.Q.	0.9266	0.8768	0.8220	0.7018	0.8137	0.8699

The changes in O_2-uptake, CO_2-evolution following the single infusion of this fat emulsion were investigated. As shown in Table 3 and Fig. 2, O_2-uptake began to increase immediately and reached its maximum 9 hours after the infusion. Then, it decreased gradually to the pre-infusion level. In this case, the value of R. Q. began to decrease and reached its minimum 6 hours after the infusion. Then, it returned to the pre-infusion value.

These experimental results which the author carried out in rabbits coincided completely with those which SHIGENAGA carried out in rats. Accordingly, we cannot help believing that fat infused intravenously in the form of emulsion can be oxidized in the body.

(iii) Infusion of 20 % Sesame Oil Emulsion Containing 7 % Glucose (Group A)

Changes in O_2-uptake, CO_2-evolution and R. Q. following the single infusion of 20 % sesame oil emulsion containing 7 % glucose in rabbits, were investigated. As shown in Table 4 and Fig. 3, a rapid increase in O_2-uptake caused mainly by oxidation of the glucose contained in the sesame oil emulsion was observed immediately after the infusion. However, O_2-uptake decreased again after a temporary but marked increase. And then, a subsequent more marked increase in O_2-uptake due to the oxidation of the fatty acids in the fat emulsion followed after the above mentioned initial rapid increase, and O_2-uptake reached its maximum 9 hours after the infusion. However, the value of R. Q. before the infusion temporarily remained as it had been, but it began to decrease eventually and reached its minimum 6 hours after the infusion.

(iv) Simultaneous Infusion of Methionine with 20 % Sesame Oil Emulsion Containing 7 % Glucose (Group B)

Recently, ARTOM and ENTENMAN have emphasized that choline, which is synthesized by methionine, promotes fatty acid oxidation in the liver. ASADA, IZUKURA and HASHINO in our laboratory demonstrated that methionine accelerated phagocytosis and the conversion into phospholipid from glyceride by the reticuloendothelial

Table 4 Changes in the value of R. Q. following single infusion of 20% sesame oil emulsion containing 7% glucose into rabbits (Group A)

Time after infusion		0	1 hr.	3 hrs.	6 hrs.	9 hrs.	12 hrs.
No. 14	O_2	16.2180	22.8000	20.1396	21.7373	24.9250	20.8993
	CO_2	15.0466	20.0400	16.6964	15.2937	20.6379	18.8194
	R. Q.	0.9277	0.8684	0.8290	0.7035	0.8280	0.9000
No. 15	O_2	11.9285	16.3064	15.7993	16.4416	18.7806	17.0560
	CO_2	10.9285	14.5398	13.1863	11.6407	16.0373	15.4214
	R. Q.	0.9166	0.8916	0.8346	0.7080	0.8538	0.9041
No. 17	O_2	11.0840	16.3870	14.5530	15.2110	17.4630	15.2110
	CO_2	10.4797	14.5923	12.1520	10.5390	14.1050	13.4000
	R. Q.	0.9454	0.8904	0.8350	0.6928	0.8076	0.8809
Mean	O_2 Change(%)	0	+ 41.73	+ 29.33	+ 36.38	+ 56.25	+ 36.38
	R. Q.	0.9299	0.8834	0.8328	0.7014	0.8264	0.8950

Fig. 3 Changes in the value of R. Q. following single infusion of 20% sesame oil emulsion containing 7% glucose into rabbits (Group A)

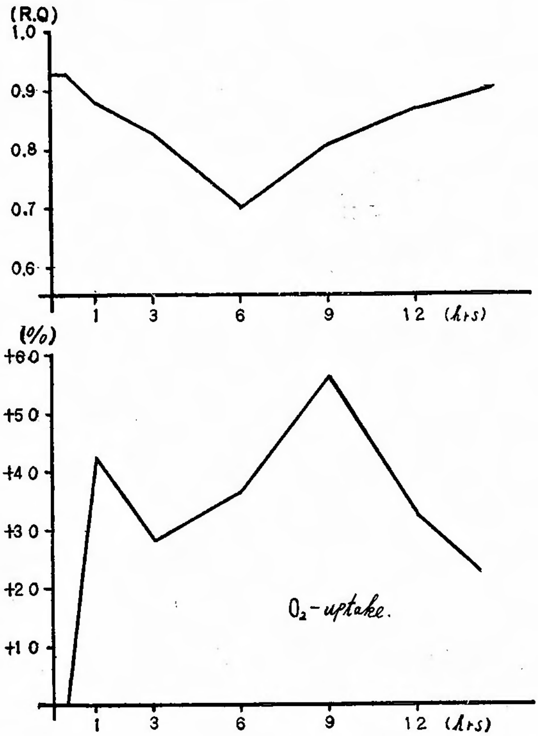
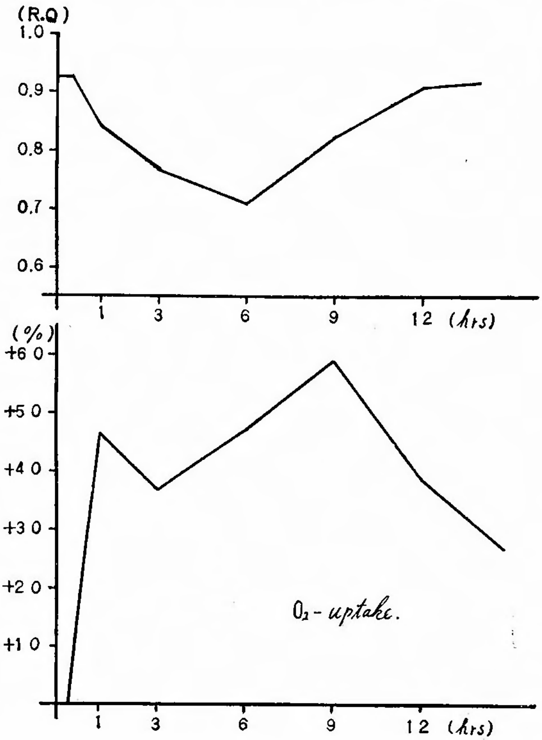


Fig. 4 Changes in the value of R. Q. and oxygen consumption following simultaneous infusion of methionine with 20% sesame oil emulsion containing 7% glucose into rabbits (Group B)



cells, and secondarily expedited fatty acid oxidation at least to the stage of ketone bodies, in the hepatic parenchymatous cells. Moreover, Kennedy et al. stated that cytidine triphosphate took part in the synthetic process of phospholipid and that the lipid acceptor of phosphorylcholine was diglyceride and was not phosphatidic acid. That is, phosphorylcholine and phosphorylethanolamine, which are produced from choline and ethanolamine, change into cytidine diphosphate choline and cytidine diphosphate ethanolamine. And then, phosphatidylcholine, which is lecithin, and phosphatidylethanolamine, which is cephalin, are synthesized from cytidine diphosphate choline and cytidine diphosphate ethanolamine in the presence of diglycerides, and cytidine monophosphate is utilized to synthesize cytidine triphosphate.

The author investigated the applicability of the above facts from the view-point of changes in total oxygen consumption and carbon•dioxide production following the simultaneous infusion of methionine with 20% sesame oil emulsion containing 7% glucose. The author injected rabbits with 0.5 g of fat plus 5 mg of *l*-methionine per kg and measured the changes in O_2-uptake, CO_2-evolution and R.Q. successively.

As shown in Table 5 and Fig. 4, results of this experiment showed clearly that throughout the time of this experiment, changes in O_2-uptake were maintained

Table 5 Changes in the value of R. Q. following simultaneous infusion of methionine with 20% sesame oil emulsion containing 7% glucose into rabbits (Group B)

Time after infusion		0	1 hr.	3 hrs.	6 hrs.	9 hrs.	12 hrs.
No. 18	O_2	15.5340	23.2330	21.2800	23.7900	24.7235	21.9450
	CO_2	14.3830	19.6020	16.4160	17.6900	20.4851	19.9500
	R. Q.	0.9259	0.8437	0.7714	0.6923	0.8285	0.9090
No. 19	O_2	16.6860	24.2481	22.9816	24.0560	26.3800	22.4400
	CO_2	15.4500	20.6540	17.7975	17.1160	22.5072	20.8800
	R. Q.	0.9259	0.8518	0.7770	0.7096	0.8148	0.9062
No. 20	O_2	14.6200	21.3400	20.0376	21.1200	23.6230	19.7800
	CO_2	13.7600	17.9450	15.1588	15.4000	19.8400	18.0600
	R. Q.	0.9411	0.8409	0.7565	0.7250	0.8400	0.9130
Mean	O_2 Change(%)	0	+ 46.82	+ 37.25	+ 47.25	+ 59.63	+ 39.18
	R. Q.	0.9319	0.8454	0.7683	0.7086	0.8277	0.9094

at a higher level than those in Group A. And the value of R. Q. in Group B began to decrease at an ealier stage than that in Group A and reached its minimum 6 hours after the infusion. These facts show that fat infused intravenously in the form of emulsion can be oxidized more smoothly in the body when methionine is used simultaneously.

(v) Simultaneous Infusion of Various Vitamins with 20 % Sesame Oil Emulsion Containing 7 % Glucose (Group C)

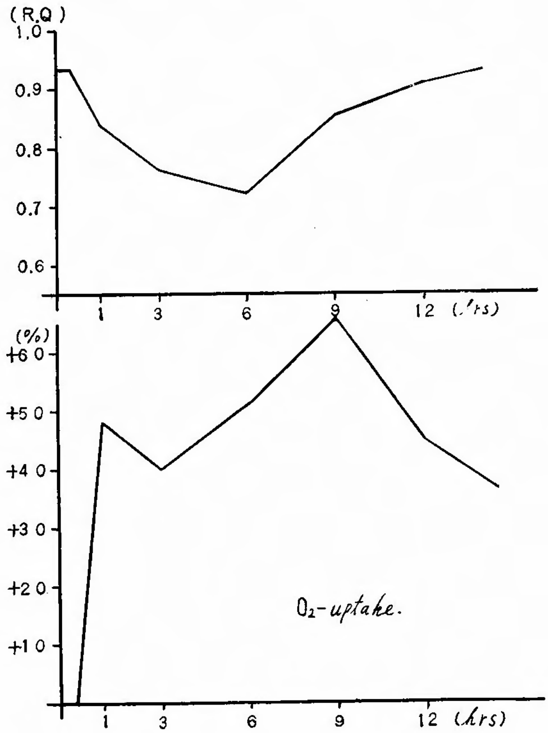
Recent in vitro biochemical studies on fatty acid oxidation by Green, Lipmann, Ochoa and Lynen etc., have shown that both pyridine nucleotides and flavoprotein play an essential role as hydrogen carriers in this metabolic process (in Fatty Acid Cycle after Lynen). Furthermore, it has been established from their in vitro studies that all hydrogen atoms, which are liberated from the T. C. A. Cycle, are

Table 6 Changes in the value of R. Q. following simultaneous infusion of methionine and various vitamins with 20% sesame oil emulsion containing 7% glucose into rabbits (Group C)

Time after infusion		0	1 hr.	3 hrs.	6 hrs.	9 hrs.	12 hrs.
No. 21	O_2	15.8400	23.5477	22.2395	23.9627	26.2278	22.9806
	CO_2	15.1200	19.7800	17.0486	17.7879	22.4064	20.9915
	R. Q.	0.9545	0.8400	0.7666	0.7419	0.8543	0.9178
No. 23	O_2	16.0182	23.6781	22.4110	24.3268	26.5549	23.2488
	CO_2	14.8232	19.9393	16.9046	17.6442	22.5132	21.0448
	R. Q.	0.9254	0.8421	0.7543	0.7253	0.8478	0.9052
No. 24	O_2	15.3120	22.6235	21.4551	23.1962	25.3658	22.2299
	CO_2	14.4400	19.0060	16.6942	16.5806	21.8957	20.3670
	R. Q.	0.9424	0.8401	0.7781	0.7148	0.8632	0.9162
Mean	O_2 Change(%)	0	+ 48.07	+ 39.97	+ 51.49	+ 65.66	+ 45.18
	R. Q.	0.9407	0.8407	0.7663	0.7273	0.8551	0.9130

carried by pyridine nucleotides, flavoproteins and cytochrome systems to combine with oxygen, and thus fatty acid is oxidized completely to water and carbon•dioxide. TSUKADA, OSA, KUYAMA and HANAFUSA in our laboratory reported that the intravenous administration of fat emulsion was made nutritiously effective by the simultaneous administration of riboflavin and nicotinic acid. It has also been demonstrated that ascorbic acid activates both aconitase and succinic dehydrogenase and is able to convert aceto-acetic acid probably to acetic acid and glycolic acid. In fatty acid oxidation, fatty acid is oxidized in the form of derivatives of coenzyme A by successive β-oxidation, and consequently is converted to acetyl-CoA, which enters into the T. C. A. Cycle by condensation with oxaloacetic acid. It has been established that in the T. C. A. Cycle, α-ketoglutaric acids is converted to succinic acid via succinyl-CoA by combination with coenzyme A and by oxidative decarboxylation. Therefore, coenzyme A plays a very important role in fat metabolism.

Fig. 5 Changes in the value of R. Q. and oxygen consumption following simultaneous infusion of methionine and various vitamins with 20% sesame oil emulsion containing 7 % glucose into rabbits (Gruop C)



Accordingly, the author attempted to explain why the metabolism of the fat emulsion is improved by the simultaneous infusion of the following drugs: 5 mg of *l*-methionine, 4 mg of vitamin B_1, 2 mg of vitamin B_2, 10 mg of vitamin C, 4 mg of nicotinic acid and 5 mg of pantothenic acid per kg. These were injected into rabbits simultaneously with the 20 % sesame oil emulsion containing 7 % glucose, and then the changes in O_2-uptake, CO_2-evolution and R. Q. were investigated. As shown in Table 6 and Fig. 5, the rate of increase in O_2-uptake was higher than that in both Group A and B throughout this experiment. On the contrary, the value of R. Q. in Group C began to decrease at an earlier stage than that in Group B and reached its minimum about 6 hours after the infusion. However, a tendency to return to the former value was more rapidly observed in Group C than in Group B.

As shown in Figs. 6 and 7, these results indicate that the infused fat is oxidized more smoothly and completely in all tissues when methionine is infused simultaneously with various vitamins in the sesame oil emulsion than when the sesame oil emulsion is given alone or with methionine only.

2) CHANGES IN VAKAT-O FOLLOWING REPEATED INFUSIONS OF FAT EMULSION

These results indicate that after a single infusion of sesame oil emulsion, the intravenously infused fat can be well oxidized in vivo. In addition, the changes in Vakat-O following repeated infusion of this fat emulsion were investigated.

(i) Changes in Vakat-O Following Repeated Infusions of 20 % Sesame Oil Emulsion Containing 7 % Glucose

Normal rabbits had been maintained on a fixed diet for more than 3 weeks so that they had attained a steady weight at the time of experiment. They were also in steady nitrogen balance. Into these rabbits, 20 % sesame oil emulsion containing 7 % glucose was infused repeatedly for 15 days, and the changes in urinary nitrogen output and Vakat-O were measured daily. As shown in Table 7, a gradual increase in Vakat-O was observed in parallel with a decrease in urinary nitrogen output with repeated infusions of this fat emulsion. Accordingly, a gradual increase in Vakat-O/N (N…quantity of nitrogen in urine) was also observed. These results suggest that the fat infused intravenously in the form of emulsion cannot be oxidized completely and some of the intermediates of fatty acid metabolism are excreted into the urine. How much glucose should be used simultaneously with the 20 % sesame oil emulsion to enable the infused fat to be oxidized smoothly and completely? In order to clarify this point, the following experiments were performed.

Fig. 6 Changes in oxygen consumption in various experimental groups following single infusion of sesame oil emulsion into rabbits

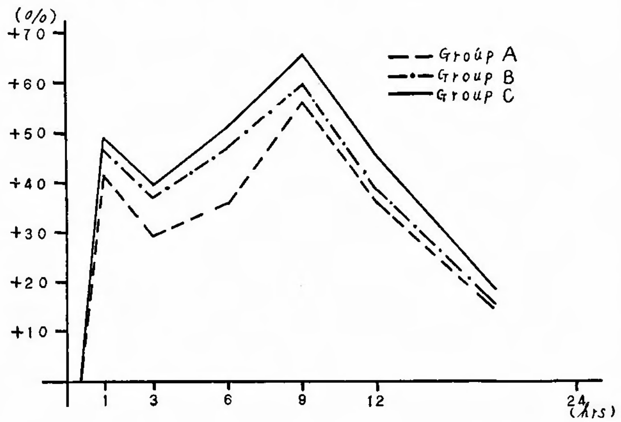
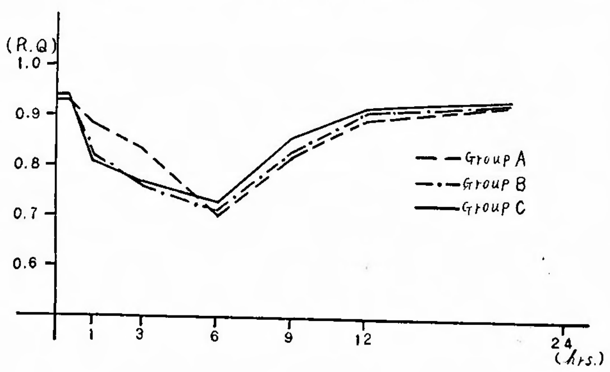


Fig. 7 Changes in the value of R.Q. in various experimental groups following single infusion of sesame oil emulsion into rabbits



(ii) Changes in Vakat-O Following Repeated Infusion of 20 % Sesame Oil Emulsion Containing 10 %, 15% or 20% Glucose

Changes in urinary nitrogen output and Vakat-O with repeated infusions of 20 % sesame oil emulsion containing 10%, 15% or 20% glucose were measured. As shown in Table 8, with infusions of 20 % sesame oil emulsion containing 10 % glu-

Table 7 Changes in Vakat-O/N in urine following repeated infusions of 20% sesame oil emulsion containing 7% glucose into rabbits (mean value)

	Days of infusion	Body weight (g)	Urinary quantity (cc/Day)	Urinary nitrogen output (g/Day)	Vakat-O (g/Day)	Vakat-O/N
No. 26	0	2050	171	1.703	0.824	0.4838
	5	2070	167	1.564	0.851	0.5441
	10	2100	159	1.381	0.829	0.6002
	15	2150	162	1.460	0.833	0.5705
No. 27	0	2250	199	1.659	1.033	0.6226
	5	2270	205	1.447	1.263	0.8728
	10	2400	190	1.444	1.117	0.7735
	15	2450	188	1.491	1.227	0.8229
No. 28	0	2550	194	1.655	0.889	0.5372
	5	2650	217	1.505	1.111	0.7382
	10	2720	203	1.579	1.294	0.8195
	15	2750	199	1.573	1.288	0.8188

cose, a gradual decrease in Vakat-O was observed. However, with infusions of fat emulsion containing 15 % glucose, a slight increase in Vakat-O was observed, and with infusions of fat emulsion containing 20 % glucose, there was a marked increase in Vakat-O. These results indicate that 10～15 % glucose should be added to the 20% sesame oil emulsion. The cause of this great increase in Vakat-O following repeated infusions of fat emulsion containing 20 % glucose can be considered to be due to the large amount of intermediates of glucose metabolism excreted into the urine.

(iii) Changes in Vakat-O Following Simultaneous Infusions of Vitamin B_1 with 20 % Sesame Oil Emulsion Containing 15 % Glucose

Table 8 Changes in Vakat-O/N in urine following repeated infusions of 20% sesame oil emulsion containing 10%, 15% or 20% glucose respectively into rabbits

	Days of infusion	Urinary nitrogen output (g/Day)	Vakat-O (g/Day)	Vakat-O/N		Days of infusion	Urinary nitrogen output (g/Day)	Vakat-O (g/Day)	Vakat-O/N
control		1.568	0.826	0.5268	20% sesame oil emulsion containing 15% glucose.	1	1.331	0.770	0.5785
		1.688	0.847	0.5017		2	1.420	0.866	0.6098
		1.451	0.783	0.5361		3	1.379	0.842	0.6105
		1.592	0.833	0.5232		4	1.370	0.829	0.6051
		1.509	0.778	0.5155		5	1.355	0.809	0.5970
	mean	1.5616	0.8134	0.5208		mean	1.3710	0.8230	0.6002
20% sesame oil emulsion containing 10% glucose.	1	1.458	0.819	0.5617	20% sesame oil emulsion containing 20% glucose.	1	1.336	0.869	0.6504
	2	1.469	0.821	0.5595		2	1.369	0.904	0.6603
	3	1.469	0.782	0.5330		3	1.361	0.868	0.6377
	4	1.417	0.771	0.5441		4	1.394	0.913	0.6549
	5	1.402	0.767	0.5470		5	1.360	0.920	0.6764
	mean	1.4430	0.7920	0.5488		mean	1.3640	0.8948	0.6560

Table 9 Changes in Vakat-O/N in urine following simultaneous infusions of vitamin B_1 with 20% sesame oil emulsion containing 15% glucose into rabbits (mean value)

	Days of infusion	Body weight (g)	Urinary quantity (cc/Day)	Urinary nitrogen output (g/Day)	Vakat-O (g/Day)	Vakat-O/N
No. 32	0	2600	204	1.770	0.984	0.5559
	5	2650	219	1.618	0.906	0.5593
	10	2750	215	1.643	0.917	0.5587
	15	2800	204	1.607	0.908	0.5650
No. 33	0	2300	169	1.380	0.856	0.6202
	5	2320	158	1.270	0.803	0.6322
	10	2370	154	1.283	0.784	0.6110
	15	2400	155	1.285	0.806	0.6272
No. 34	0	2800	227	1.541	0.883	0.5730
	5	2850	199	1.471	0.861	0.5853
	10	2900	197	1.426	0.857	0.6009
	15	2950	200	1.456	0.868	0.5961

These results show that in vivo carbohydrate metabolism must be made more smooth in order to increase the nutritious effect of the infused fat. Therefore, simultaneous use of 4 mg of vitamin B_1 per kg was made. In this case, a slight decrease in Vakat-O was observed in parallel with that in urinary nitrogen output. These results indicate that both fat and glucose infused simultaneously can be oxidized smoothly without producing any metabolic intermediates when 20 % sesame oil emulsion containing 15 % glucose is repeatedly infused with vitamin B_1 (Table 9).

(iv) Changes in Vakat-O Following Simultaneous Infusion of Various Vitamins with 20 % Sesame Oil Emulsion Containing 15 % Glucose

Fat metabolism in vivo was improved by the simultaneous infusion of *l*-methionine,

Table 10 Changes in Vakat-O/N in urine following simultaneous infusions of methionine and various vitamins with 20% sesame oil emulsion containing 15% glucose into rabbits (mean value)

	Days of infusion	Body weight (g)	Urinary quantity (cc/Day)	Urinary nitrogen output (g/Day)	Vakat-O (g/Day)	Vakat-O/N
No. 35	0	2700	323	1.982	1.087	0.5484
	5	2750	298	1.798	1.002	0.5572
	10	2800	290	1.769	0.989	0.5590
	15	2870	266	1.702	0.945	0.5552
No. 36	0	2800	312	1.851	0.994	0.5370
	5	2850	257	1.732	0.923	0.5329
	10	3000	232	1.610	0.880	0.5465
	15	3000	253	1.643	0.882	0.5368
No. 37	0	2400	206	1.566	0.812	0.5185
	5	2450	203	1.464	0.771	0.5263
	10	2550	202	1.438	0.747	0.5194
	15	2600	208	1.440	0.749	0.5201

Table 11 Changse in Vakat-O in various experimental groups following repeated infusions of sesame oil emulsion into rabbits

Days of infusion	0	5	10	15
20% Sesame oil emulsion containing 7% glucose.	—— %	+ 16.83	+ 18.09	+ 21.62
20% Sesame oil emulsion containing 15% glucose.	—— %	+ 1.23	+ 0.46	+ 0.25
20% Sesame oil emulsion containing 15% glucose + Vitamin B_1	—— %	− 5.45	− 6.06	− 5.10
20% S. O. E. (15%G) + Vit. B_1 + Vit. B_2, + Vit.C + Methionine + Nicotinic Acid + Pantothenic Acid	—— %	− 6.68	− 9.09	− 10.71

vitamin B_2, vitamin C, nicotinic acid and pantothenic acid. Therefore, changes in Vakat-O following repeated infusions of fat emulsion with various vitamins were investigated. In this case, the decrease in both Vakat-O and urinary nitrogen output was greater than with infusions containing added vitamin B_1 only (Table 10 and 11). These results show that the simultaneous use of glucose and various vitamins mentioned above is most desirable in the intravenous administration of fat emulsion. That is, the catabolic process of fat metabolism in vivo is carried out smoothly and completely when there is a simultaneous administration of the correct amount of glucose, methionine, vitamin B_1, vitamin B_2, vitamin C, nicotinic acid and pantothenic acid. When these additions are made, the administration of this fat emulsion is most effective in sparing protein and maintaining weight.

3) THE AMOUNTS OF PROTEIN, FAT AND CARBOHYDRATE METABOLIZED IN THE BODY FOLLOWING REPEATED INFUSIONS OF SESAME OIL EMULSION

Matsuda in our laboratory reported that animals well adapted to fat feeding can utilize most effectively and smoothly their storage fat or fat administered by mouth. These fat-adapted animals can prevent the rapid depletion of their carbohydrate reserve, make milder the stress effect of fasting, lessen protein catabolism and consequently maintain their liver and adrenal functions well during a fast. Moreover, Hanafusa in our laboratory reported that not only postoperative but also preoperative administration of fat emulsion is a most reasonalbe procedure for the purpose of minimizing metabolic disorders and the breakdown of body protein which affects patients after operation, especially in cases of gastrectomy after which patients must undergo a certain period of fasting and poor nutrition. And he considered that the protein sparing effect gained clinically by preoperative use of fat emulsion is induced partly by its fat-adapting action.

Thereupon, the following experiments were also performed. Changes in Vakat-O, urinary nitrogen output, oxygen consumption and carbon•dioxide production following repeated infusions of large amounts of fat emulsion (1.0 g of fat per kg) were measured. Given the total oxygen consumption, carbon•dioxide production, and urinary nitrogen elimination for a certain period, it is possible to calculate the amounts of protein, fat and carbohydrate metabolized in the body during that period. From this view-point, the author investigated the phenomenon of adaptation to fat feeding.

In this experiment, 10 mg of *l*-methionine, 8 mg of vitamin B_1, 4 mg of vitamin B_2, 20 mg of vitamin C, 8 mg of nicotinic acid and 10 mg of pantothenic acid per kg were administered simultaneously for 15 days.

Table 12 Changes in the amounts of protein, fat and carbohydrate following repeated infusions of sesame oil emulsion into rabbits

Days of infusion		Body weight (g)	Urinary nitrogen output. (g/day)	Vakat-O (g/day)	Vakat-O/N	R.Q.	% of total heat produced by		
							Protein	Fat	Carbo-hydrate
No. 38	0	2700	1.796	1.119	0.6230	0.9080	33.20	6.39	60.41
	5	2800	1.652	1.213	0.7342	0.8805	21.51	24.16	54.25
	10	2850	1.583	1.002	0.6329	0.8656	20.40	28.84	50.76
	15	3000	1.475	0.998	0.6766	0.8455	19.96	32.24	47.80
No. 39	0	2900	1.834	1.001	0.5458	0.9023	26.44	5.77	67.79
	5	2950	1.682	1.481	0.8805	0.8771	17.04	27.08	55.88
	10	3000	1.588	1.324	0.8336	0.8441	19.21	37.00	43.79
	15	3070	1.429	0.987	0.6906	0.8233	18.16	44.97	36.87
No. 40	0	2550	1.724	0.965	0.5545	0.9275	29.07	1.61	69.32
	5	2600	1.582	1.047	0.6618	0.8771	20.66	24.77	54.57
	10	2620	1.577	1.120	0.7102	0.8696	20.37	27.47	52.16
	15	2680	1.438	1.004	0.6981	0.8506	19.47	32.49	48.04

With repeated infusions of such a large amount of fat into rabbits which have little ability to dispose of fat, Vakat-O decreased again after a temporary slight increase. This result suggests that all the infused fat cannot be oxidized completely and at least a part of the infused fat is excreted into the urine as intermediates of fatty acid metabolism at the beginning of repeated infusions. However, rabbits eventually adapted themselves well to fat feeding, and urinary nitrogen output decreased gradually. Accordingly, a marked protein sparing effect was brought about. The above mentioned facts can be better understood when the amounts of protein, carbohydrate and fat metabolized in the body with repeated infusions of fat emulsion are calculated from the O_2-uptake, CO_2-evolution and urinary nitrogen output for that period. That is, a gradual decrease in the amount of carbohydrate and protein metabolized in the body was caused by the fat-adapting effect. Accordingly, the author reached the following conclusion. The intravenous administration of our fat emulsion shows a great protein and carbohydrate sparing effect, when the correct amounts of glucose, methionine, vitamin B_1, vitamin B_2, vitamin C, nicotinic acid and pantothenic acid are used simultaneously (Table 12).

IV. SUMMARY AND CONCLUSION

The present experiments were carried out to determine whether or not the sesame oil emulsion produced in our laboratory shows any marked protein and carbohydrate sparing effect on intravenous infusion into normal rabbits, and to observe from the changes in oxygen consumption, Vakat-O, Vakat-O/N, and the amounts of the three main foodstuffs metabolized in the body for a certain period whether or not glucose and various vitamins, which have been found recently to show biochemical activity in vitro, are of any significance in vivo.

The author reached the following conclusions.

1) The catabolic process of fat metabolism in vivo was carried out smoothly and completely with the simultaneous administration of glucose, methionine and various vitamins, such as thiamin, riboflavin, ascorbic acid, nicotinic acid and pantothenic acid.

2) Accordingly, the simultaneous use of these drugs with 20 % sesame oil emulsion is most desirable. In that case, the fat infused intravenously in the form of emulsion for the purpose of parenteral nutrition is utilized most effectively.

3) A marked protein and carbohydrate sparing effect following repeated infusions of large amounts of fat emulsion is induced by the fat-adapting function of the body.

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ガス代謝の面からする経静脈性脂質輸入の意義についての実験的研究

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教室創製の静脈内注入可能な脂質乳剤を家兎に注入し，その際のガス代謝，尿中窒素排泄量，及び Vakat-O 更に三大栄養素燃焼比率を測定し，次のような結果を得た．

1) 脂質乳剤を1回限り静脈内へ注入すると呼吸商は時間の経過と共に低下し，6時間後に最低の 0.7 前後の値を示し，その後再び上昇して注入前の値に復するのに対して酸素消費量は注入後漸次増大し，9時間後に至つて最高潮に達し，その後は次第に減少して注入前値に復する．

2) 脂質乳剤と共にメチオニン及びパントテン酸，ニコチン酸アミド，ビタミンB_1，ビタミンB_2，ビタミンCを併用すると，呼吸商の低下は更に速やかとなり，酸素消費量もより一層著明に増加する．

3) 以上の事実は脂質を乳化態として静脈内へ注入しても，注入脂質がよく熱源的効果を発揮することを示唆している．

4) Vakat-O の消長からみて 20%ゴマ油乳剤中には10%～15%の割合にブドーを添加することが望ましい．併しこのブドーの添加量が過大に過ぎる時は，Vakat-O は再び増大する傾向を示す．

5) 10%～15%ブドー糖含有ゴマ油乳剤の注入に当つても，メチオニン，パントテン酸，ニコチン酸アミド，ビタミンB_1，ビタミンB_2，ビタミンCを併用投与する時は，注入脂質の熱源的効果は更に倍加され得るものと思考される．

6) 脂質乳剤の大量を反覆注入すると，Vakat-O は注入開始直後1時的乍ら増大するが，注入日数の経過と共に次第に注入前値に復する．また生体内三大栄養素燃焼比率についてみると注入開始後より脂質燃焼率は可成り増大し，注入日数の経過と共に益々増大し，蛋白質，糖質の燃焼率は減少する．

7) 従つて脂質が大量に投与されると，個体は脂質利用に最も好適な体内環境を自ら形成する適応現象を示すものであり，これによつて著明な蛋白質，並びに糖質の節約作用が招来される．